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Application No.: RCE of 10/055,075

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: **Torabinejad and Johnson**	Confirmation No.:
Application No.: **RCE OF 10/055,075**	Group Art Unit: **1614**
Filing Date: **Herewith**	Examiner: **Donna Jagoe**
For: **Irrigation Solution and Methods for Use**	

DECLARATION OF RICHARD E. BELTZ, Ph.D.

Dr. Richard E. Beltz hereby declares:

I received a Ph.D. in Biochemistry and Nutrition from the University of Southern California in 1956. From 1956 through 1970, I held academic appointments of Instructor, Assistant Professor, Associate Professor, and, finally, Professor of Biochemistry in the School of Medicine, Loma Linda University, Loma Linda, CA. From 1960 through 1964, I was a National Cancer Institute Senior Research Fellow and Career Development Awardee at the Loma Linda University School of Medicine.

From 1970 through 2000, I was Professor of Biochemistry, Loma Linda University School of Medicine. I formally retired July 1, 2000, but remained active in research and consulting. In October, 2000, I received a lifetime appointment as Emeritus Professor of Biochemistry and Microbiology, Division of Biochemistry, Loma Linda University School of Medicine.

I am aware of the patent application, U.S. Serial No. 10/055,075 (the "075 Application") in the name of Torabinejad and Johnson. The 075 Application discloses endodontic and other rinses having organic acids present in the solutions at levels of 0.5% to 10%, specified as weight/volume. Such organic acids are said preferably to have pK_1 values between 1.5 and 5. Knowing the ionization constant (K_1) of a monobasic organic acid allows an accurate calculation of the pH value of a dilute aqueous solution containing that acid at any specified

concentration. The highest pH value (weakest acidic solution) is obtained from compositions having the lowest concentration of the weakest acid. The lowest concentration of acid is 0.5 % (wt./vol.). The acids for the inventive compositions are characterized as having a pK_1 from 1.5 to 5. Further, the specification provides a list of exemplary organic acids such as citric, chloracetic (mono), maleic, saccharic, tartaric, and acrylic (monomer of polyacrylic).

Assuming 0.5 % (wt./vol.) of acid, I have calculated the pH values of solutions of the listed, preferred organic acids. They appear in the last column of the following table:

Organic Acid	**K_1[b,d]**	**pK_1[d]**	**Mol. Wt.**	**pH of 0.5% (wt./vol.) solution**
Maleic	1.17×10^{-2}	1.93[c]	116.07[a]	1.80
Chloracetic (mono)	1.55×10^{-3}	2.81[c]	94.50[a]	2.08
Tartaric	1.3×10^{-3}	2.98[a]	150.09[a]	2.23
Citric	8.2×10^{-4}	3.128[a]	192.13[a]	2.38
Acrylic	5.6×10^{-5}	4.25[a]	72.06[a]	2.72
Saccharic	1.0×10^{-5}	5.00[c]	210[b]	3.35

[a]Merck Index, 12th Edition
[b]Dictionary of Organic Compounds, 4th Edition, Eyre and Spottiswoode (Publishers) Ltd., London (1965)
[c]Calculated from K_1 value listed
[d]25 °C

The calculation of pH is as follows:

Ionization of a monobasic organic acid, HA: $HA \rightleftharpoons H^+ + A^-$

$[H^+] \times [A^-] / [HA] = K_1$

Brackets signify molar concentration. [HA] is the concentration of undissociated acid molecules in the aqueous solution.

Let X = concentration of each ion in solution

Let [HA] = ([total acid] – X)

Then, X^2 / ([total acid] – X) = K_1

This equation is rearranged into a quadratic equation, which is then solved for X, the hydrogen ion concentration:

$$X^2 + K_1(X) - K_1([\text{total acid}]) = 0$$

Finally, pH = log 1/X

These formulas apply fairly well also to di- and tribasic acids, because the latter dissociate in steps. The first hydrogen atom ionizes (or dissociates) much more readily than the second or third in a polybasic acid, so the first ionization essentially determines the pH of a polybasic organic acid in solution.

The following is exemplary of the calculations I used to determine the foregoing pH values:

For citric acid:

5.0 g / 1 L (0.5 % wt./vol.)

$$X^2 + 8.2 \times 10^{-4}(X) - 8.2 \times 10^{-4}(0.0260 \text{ molar}) = 0$$

Solving this equation for X: $X = 4.187 \times 10^{-3}$

$1/(4.187 \times 10^{-3}) = 238.8$

log 238.8 = pH = 2.38

As each of the calculations was performed for the lowest concentration of organic acid in solution, 0.5% (wt./vol.), use of higher concentrations of acid will necessarily confer stronger acidity upon the solution, reflected by lower pH values than are attained with the respective 0.5% (wt./vol.) solution.

I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further, that these statements were made with the knowledge that willful false statements and the like so made

are punishable by fine or imprisonment, or both, under § 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: Nov. 22, 2005

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